



Trichomoniasis in Adolescents: Unsuspected and Neglected

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Ode to the south

“Ever since locating here in the south
I have had barbecue sauce on my mouth”

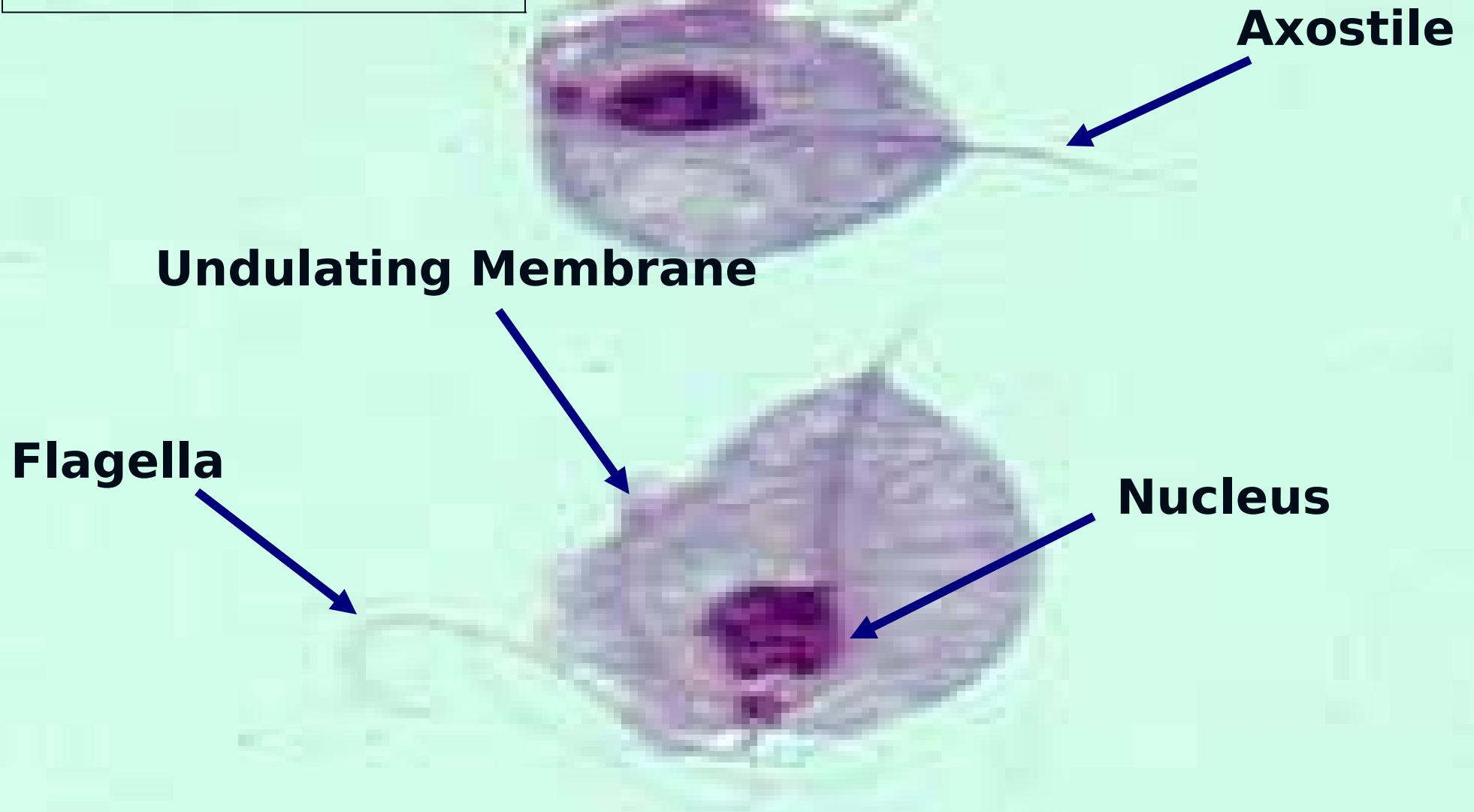
Roy Blount, Jr.



Objectives

- Review Pathobiology of *Trichomonas vaginalis*
- Evaluate prevalence of TV infection
- Discuss outcomes associated with TV
- Compare diagnostic methods
- Update on research in Adolescent Women
- Future directions for research and practice

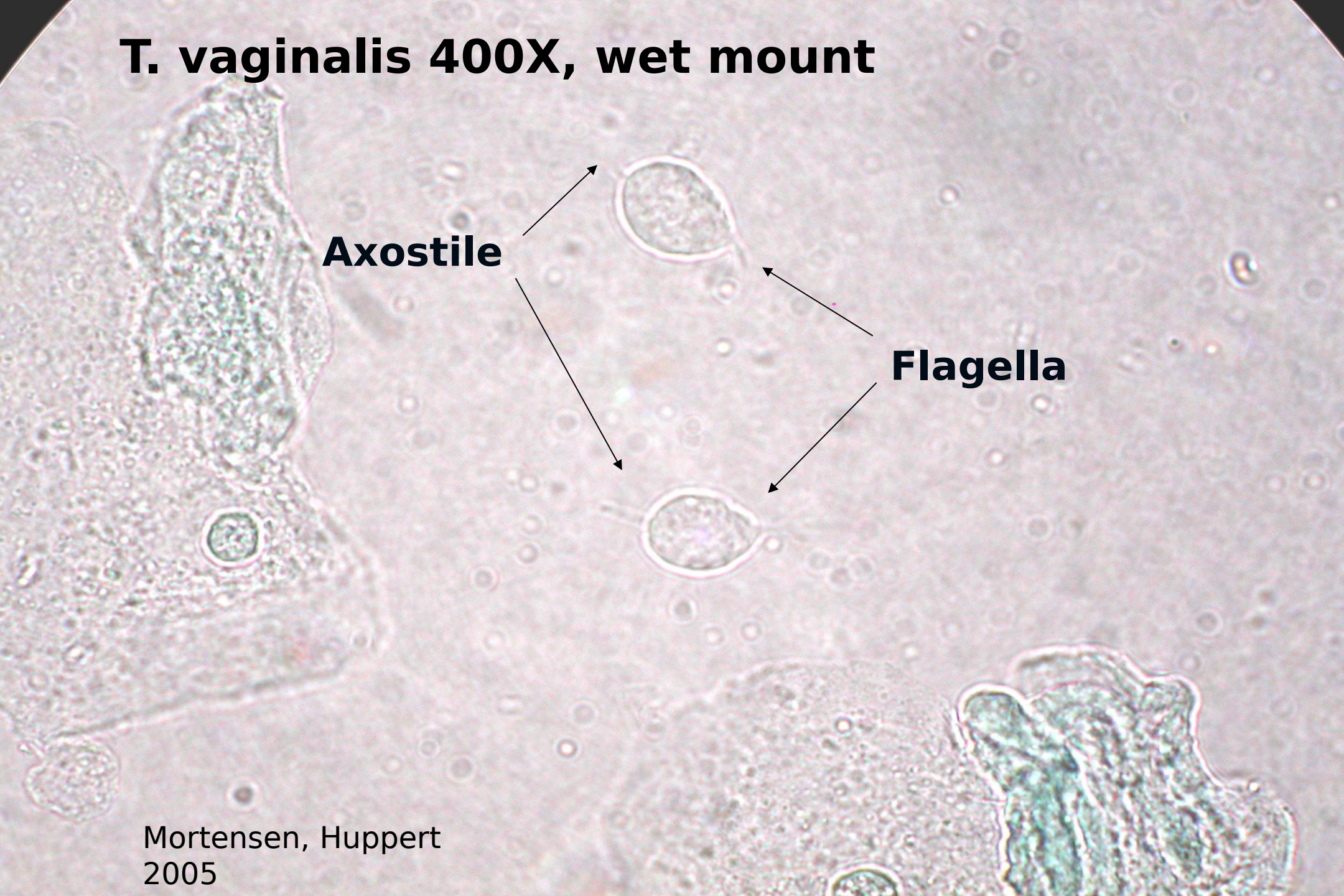
Giemsa stain

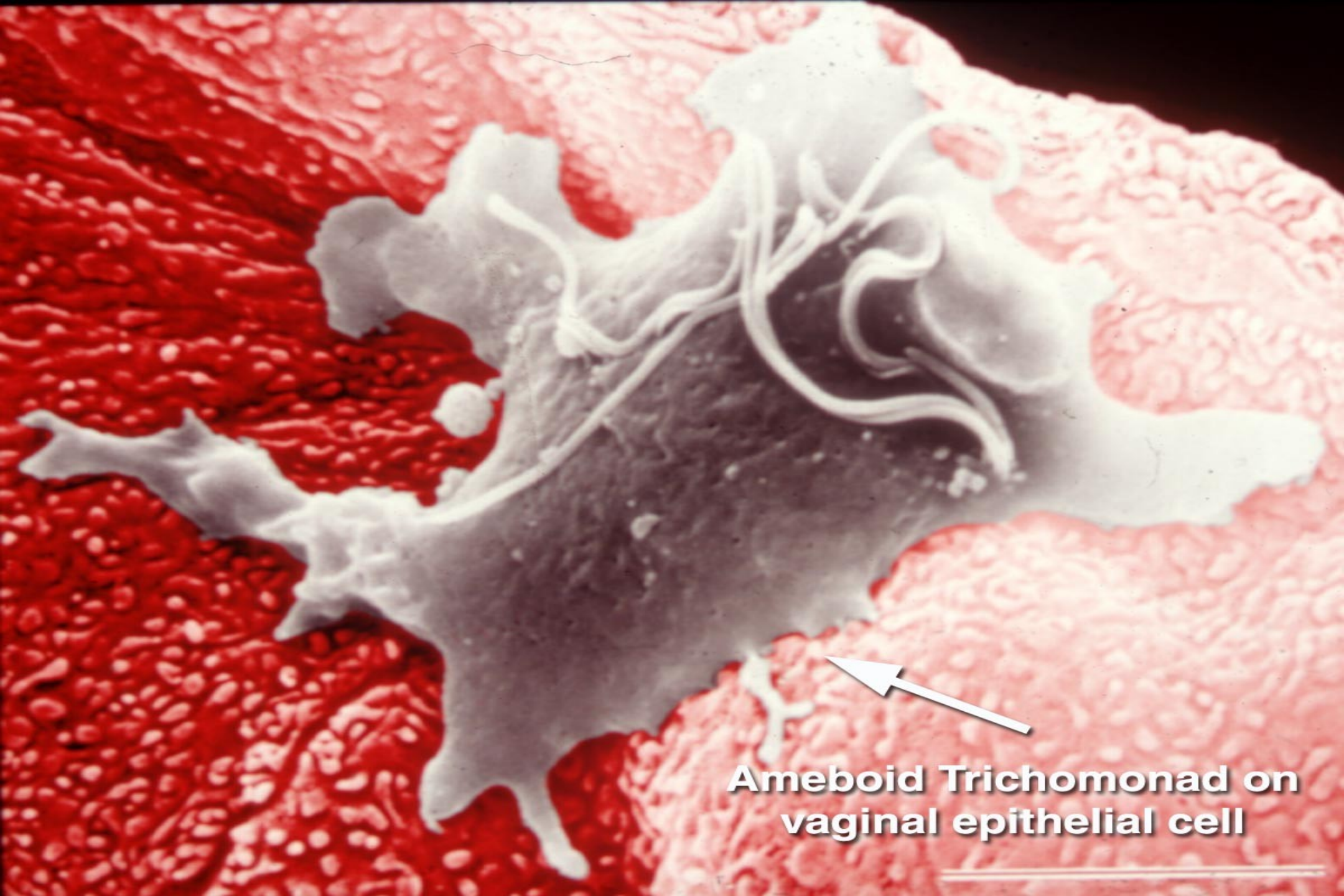


T. vaginalis 400X, wet mount

Axostile

Flagella





**Ameboid Trichomonad on
vaginal epithelial cell**



Trich pathobiology

- Inoculation
- Adhesion
- Local damage
- Inflammatory response
- Prolonged survival:
 - Alter host flora and pH
 - Avoid immune detection
 - Acquire nutrients



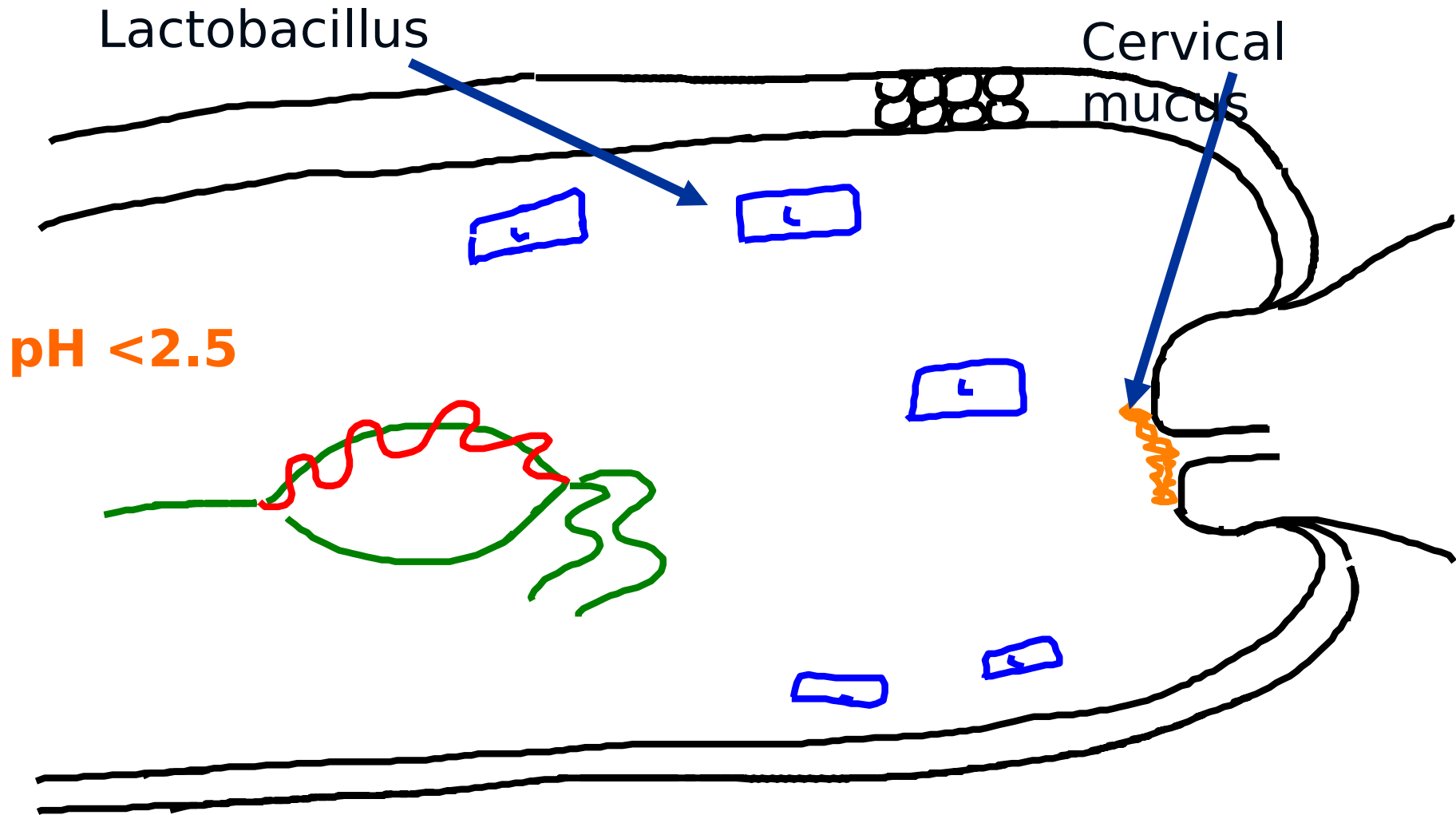
Inoculation

- Sexual contact
- Incubation 4-28 days
- Long duration of infection
 - 4 months in men
 - 5 years in women (Bowden, 2000)
- Prevalence increases with age

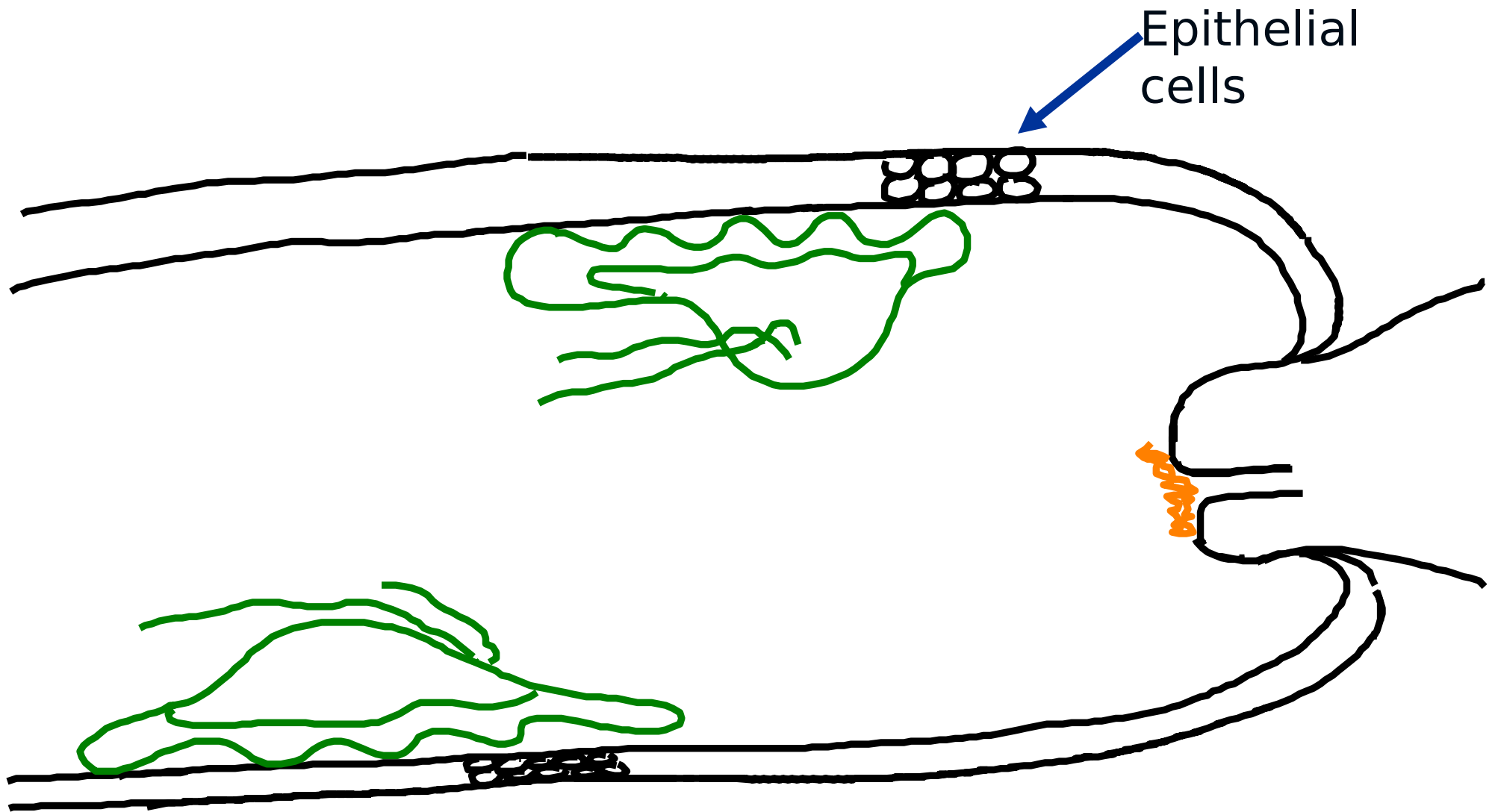


Transmission

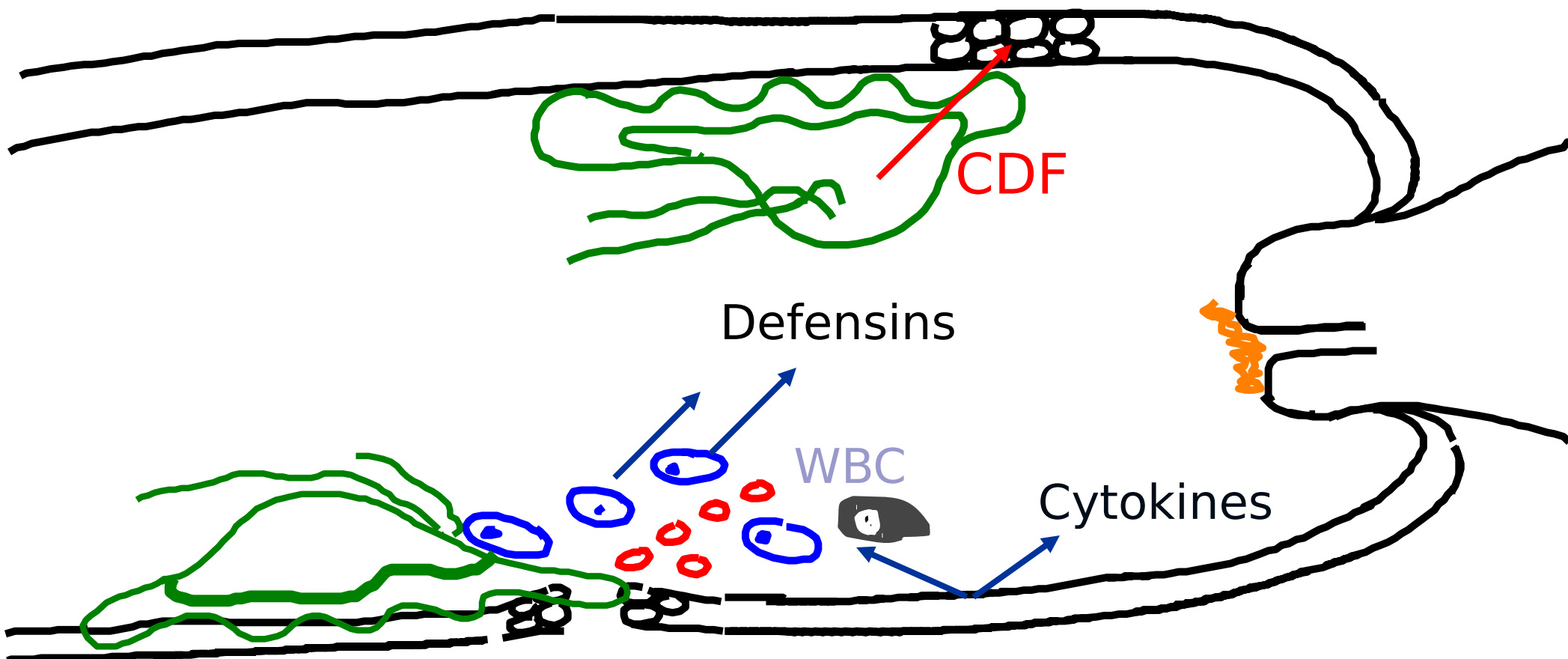
- More easily transmitted than CT, NG, HIV....
- Male to female: 85%
- Female to male:
 - 20-60% (Krieger, 1995)
 - 70% (Sena, 2003)



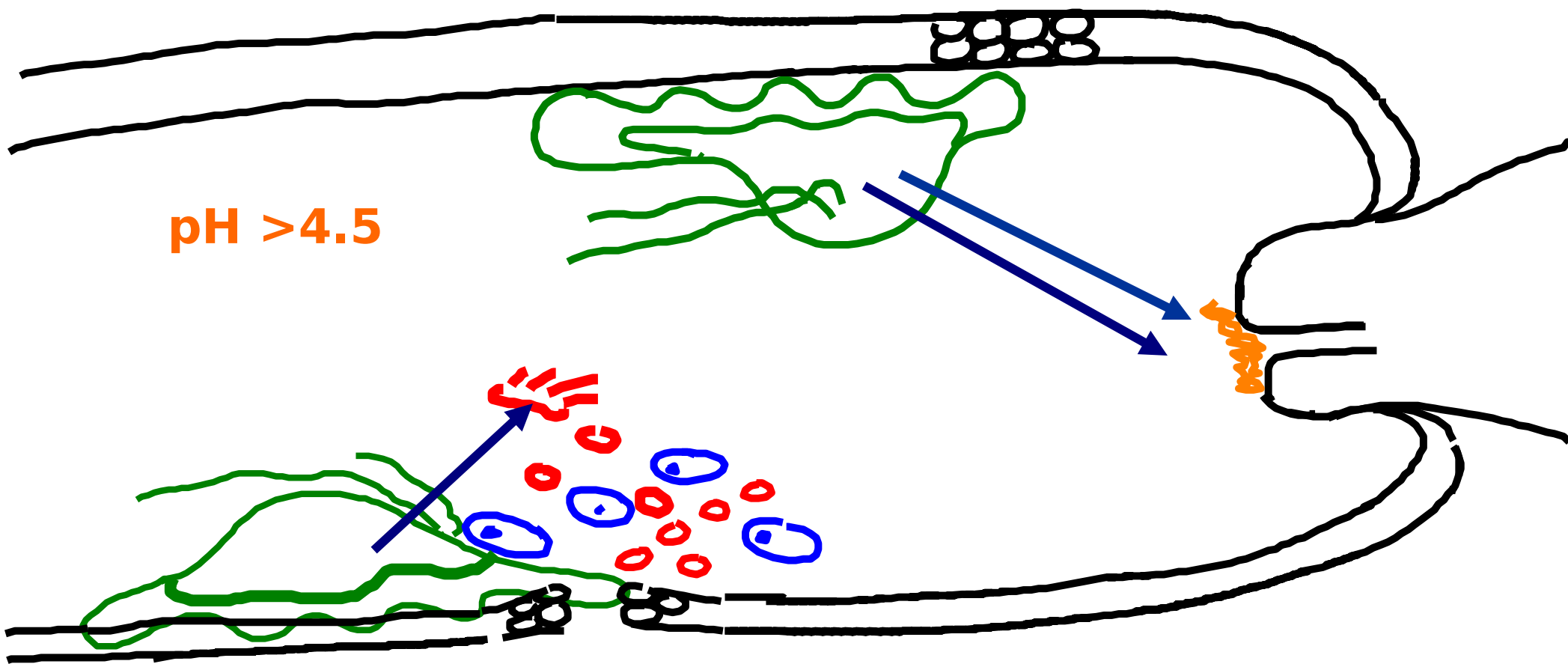
Trich inoculates the vagina



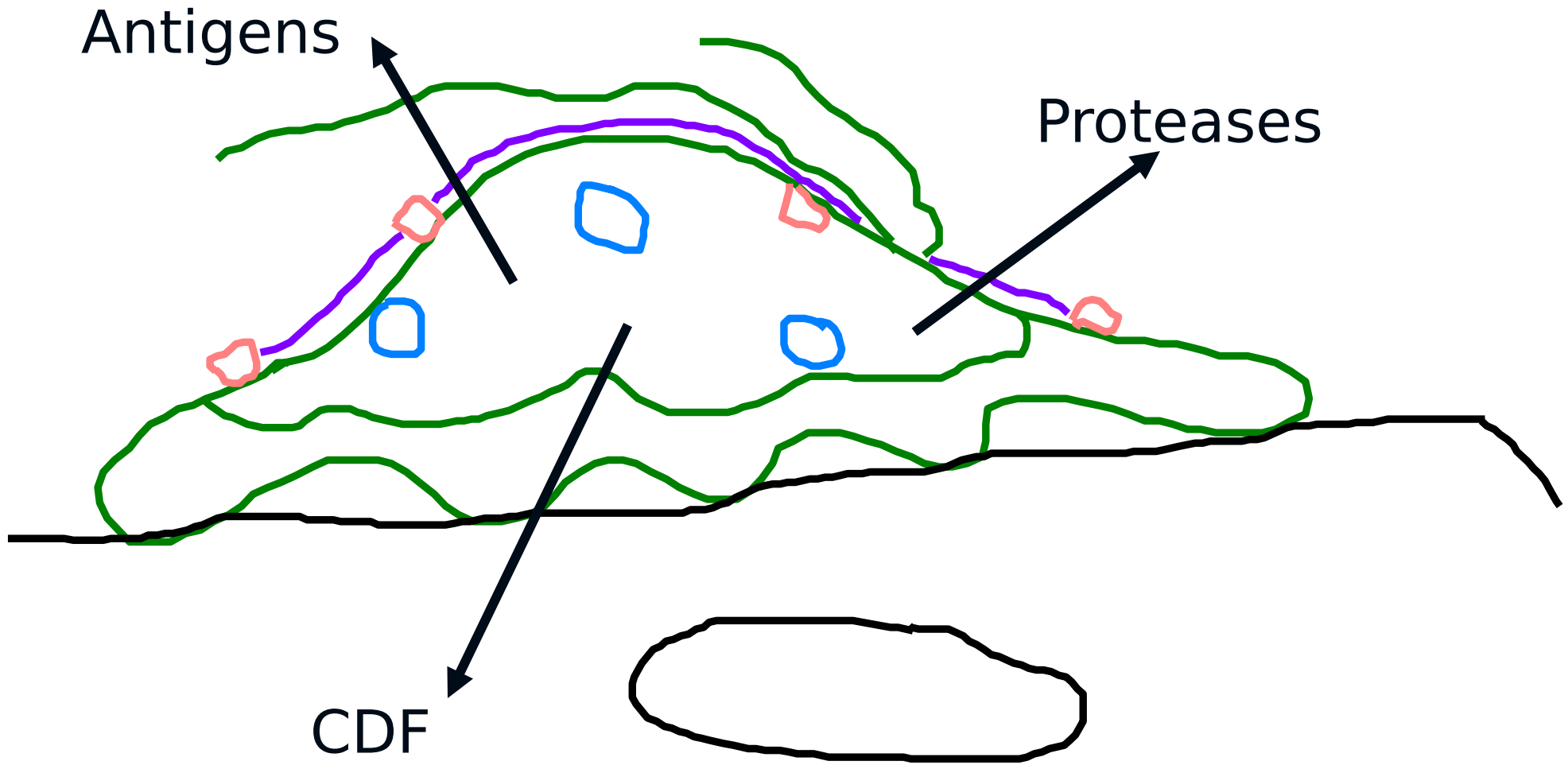
Trich adheres to the vagina



Local Damage and Host response



Acquire nutrients




Trich: attached and persistent

Trich: Highly prevalent

- Most common non-viral STD
- More common than CT and GC
- Worldwide > 180 million cases / year
- US estimated 7.4 million cases in 2000

Cates, 1999

Weinstock,
2004



Prevalence estimates are limited by:

- Rare population testing (1 study)
- No reporting requirements
- No tracking of in-office tests
- No screening guidelines
- Low sensitivity of usual diagnostic method (wet mount)

Trich prevalence (cont):

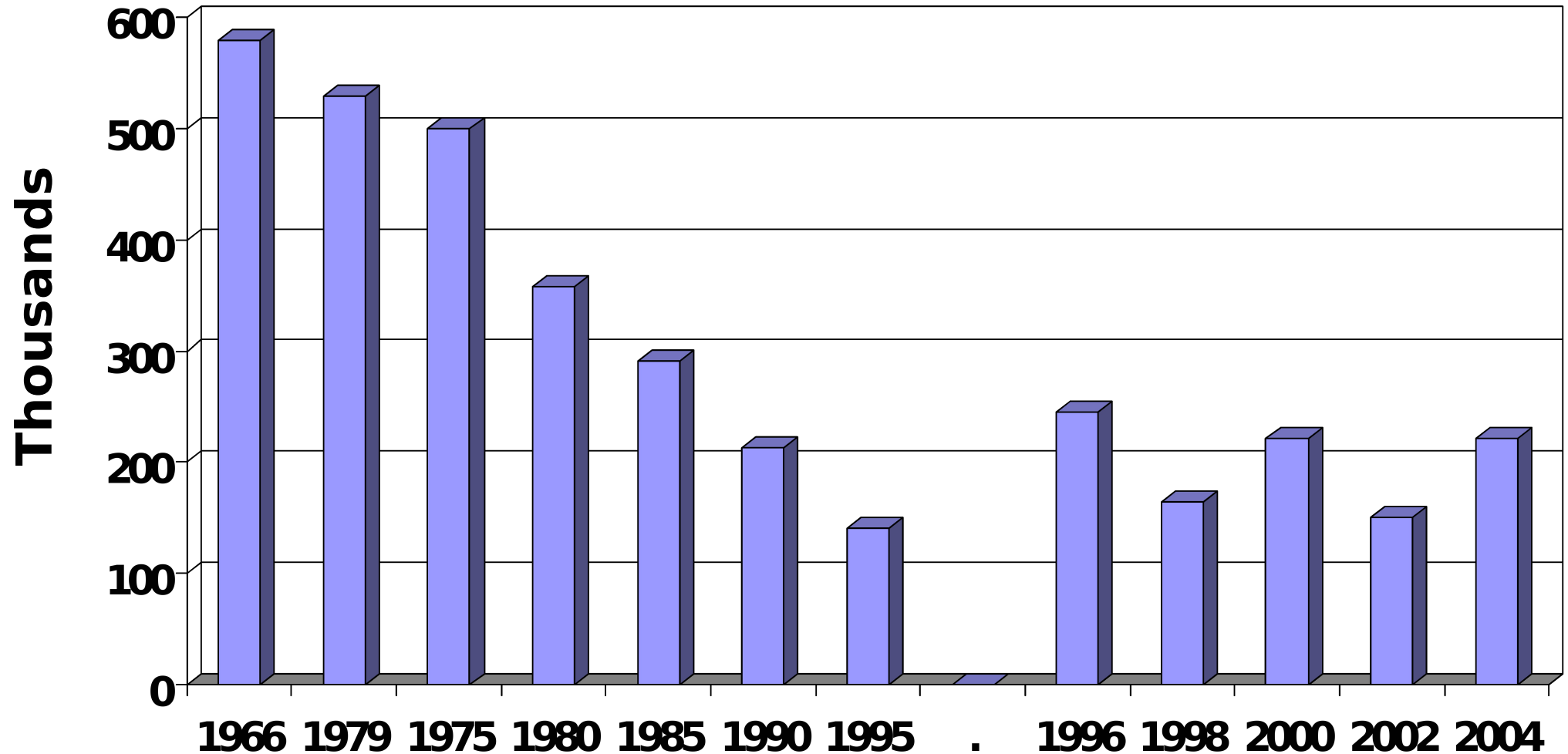
- No screening guidelines
 - Asymptomatic subjects not tested
 - >50% of those infected with TV may be asymptomatic
- Low sensitivity of common diagnostic methods
 - Wet mount 60% sensitive
 - Pap smear 60% sensitive

Wolner-Hanssen, 1989

Weise, 2000

Lara-Torre, 2003

TV prevalence, US women NDTI



Tv Prevalence in US Young Adults

- National Long. Study of Adolescent Health
 - Wave 3, Age 18-26
 - N=12,449
 - Nationally representative
- Urine sample: PCR for TV, CT, GC
- Overall **2.3%** prevalence TV
 - CT: 4%
 - GC: 0.5%

Miller, Swygard, Hobbs
et al 2005

Tv Prevalence in US Young Adults

- Race/gender disparities:

- ☐ AA women: **10.5%**
- ☐ AA men: 3.3%
- ☐ White men: 1.3%
- ☐ White women: 1.1%

- Highest: Age > 25: 4 %

- South: 2.8%

- >95% of those with TV denied symptoms

Miller, Swygard, Hobbs
et al 2005

TV Prevalence in women

Population	Author, Year	TV %
Student Health clinic	Weisenfeld, 2001	10
	Smith, 2001	13
STD Clinic	Fouts, 1980	32
	Kaydos, 2002	17
	Huppert, 2005	29
Prenatal clinic	Cotch, 1997	18
Substance abuse	Bachman, 2000	43
Prison inmates	Shuter, 1998	47



Why care about trich?

- Cute
- Prevalent
- Persistent
- Associated with bad outcomes



In Women, TV associated with ↑

- **HIV**

- Risk of other STDs (**HSV**)
- Cervical neoplasia, **HPV**
- Tubal infertility
- Post-hysterectomy infection
- Atypical PID
- Preterm birth

TV and HIV: Prevalence

- In African cities, cross sectional study
 - Low HIV (4-8%) = Low TV (3-17%)
 - High HIV (31-35%) = High TV (29-34%)
- Pregnant Congolese:
 - HIV-: TV 10%
 - HIV+: TV 18.6%

Buve, 2001
Sutton, 1999

TV and HIV Acquisition

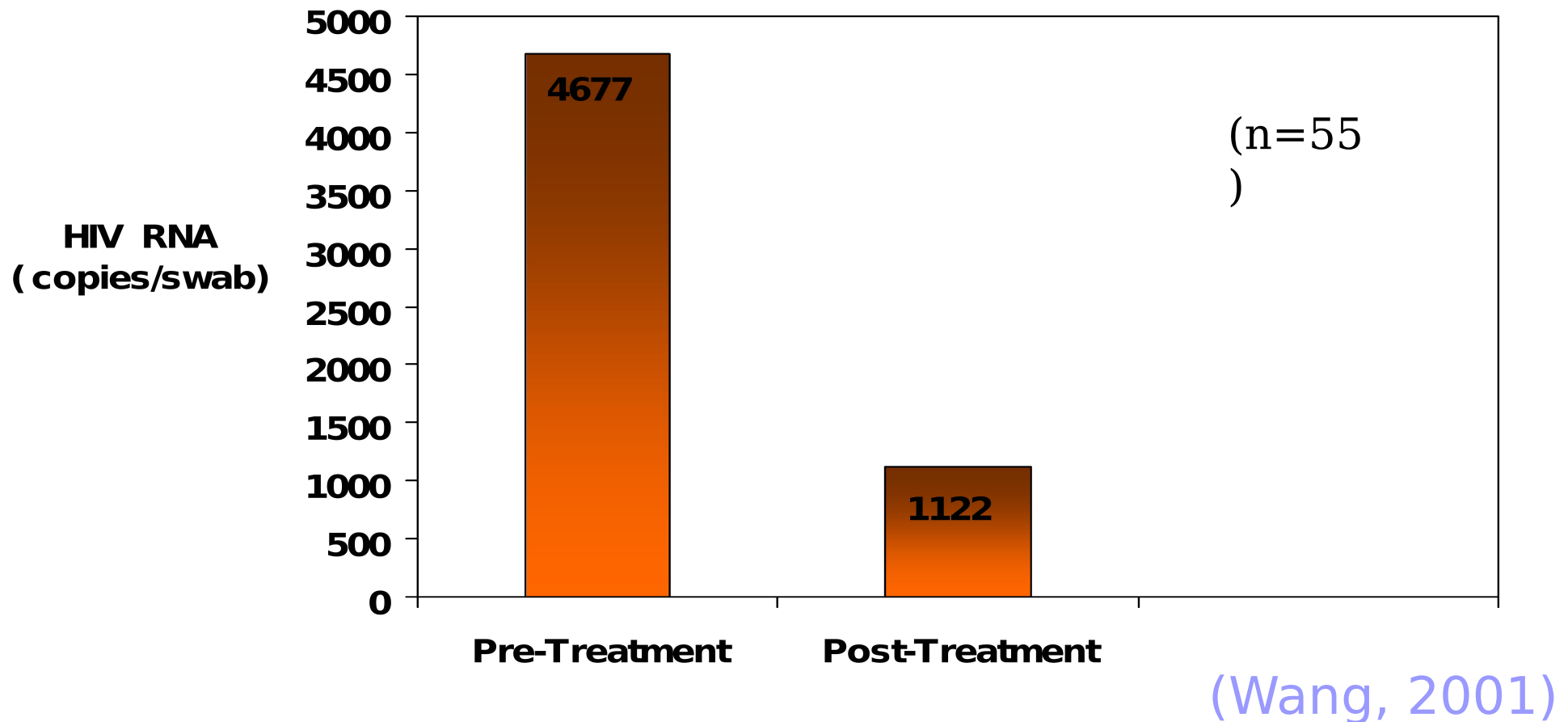
- TV associated with HIV infection
 - 431 HIV- women sex workers (Zaire)
 - With TV: OR HIV 1.9 (Laga, 1993)
- HIV associated with TV infection
 - 292 HIV+ women (US)
 - 10% annual incidence TV
 - cf 1-2% CT/GC (Minkoff, 1999)



TV as Risk Factor for HIV Transmission

- Marker for unsafe sex
- Increase susceptibility
- Increase infectiousness
- Alter normal flora and immune response

Treatment of *TV* reduces HIV in vaginal secretions





TV as a risk factor for other STDs

- GC (CT in Ad Health)
- HSV (new!)
- Cervical cancer (persistent HPV)

TV predicts GC

Study	Population	% with GC		
		TV+	v	TV -
Fouts, 1980	400 sx women	37	v	22
Wolner-Hanssen, 1989	779 women	31	v	11
Huppert, 2004	92 sx teens	61	v	17

$P < 0.01$ for each study

TV and Herpes (HSV-2)

- Cross-sectional study
- 1780 women in STD clinic
- Tests for HSV-2 serology, CT, GC and TV
 - TV dx: WM or culture
- HSV-2 + serology higher in those with hx TV
 - 74 vs 44%, $p < 0.01$
- Odds HSV-2
 - History TV: OR 1.6 (95% CI 1.2-2.2)
 - Current TV: OR 1.5 (95% CI 1.2-2.2)

TV and HSV-2

- Longitudinal follow- up of those seronegative
- 646 females
- Incident TV increased risk of HSV
- Hazard ratio=3.7 (2.0-7.1)
- Controlled for age, race, enrollment site, condom use

Gottlieb, 2004



TV and Cervical Neoplasia

- Meta-analysis of 24 studies
- Summary relative risk was 1.93
- Most case-control studies had a positive association
- Limitations
 - Retrospective
 - Sexual risk behaviors
 - Other Infections

Zhang, 1994

TV as a Risk Factor for Cervical CA

- 19,114 Finnish women
- Mass screening program for cervical ca
- Pap diagnosis of HPV, Herpes, *TV*
- *TV prevalence* 8%
- Cervical cancer associated with
 - *TV* (OR=6.4)
 - HPV (OR=5.5)



Trich Diagnostic Methods: Usual care

- Wet Mount
- Pap smear
- Limitations:
 - Low sensitivity 36-70%
 - Resources
 - Technical experience
 - Pelvic exam ?



Trich Diagnosis: Newer Methods

- Culture
- DNA probe
- PCR/ NAAT
- Rapid antigen tests



Trich Culture: InPouchTV

- Single pouch provides transport, cultivation and evaluation
- 85% sensitive 100% specific
- Self-obtained vaginal swabs can be used
- Long shelf Life
- Limitations:
 - Availability
 - 3- 5 days for final read

Borchardt, 1997

Levi, 1997

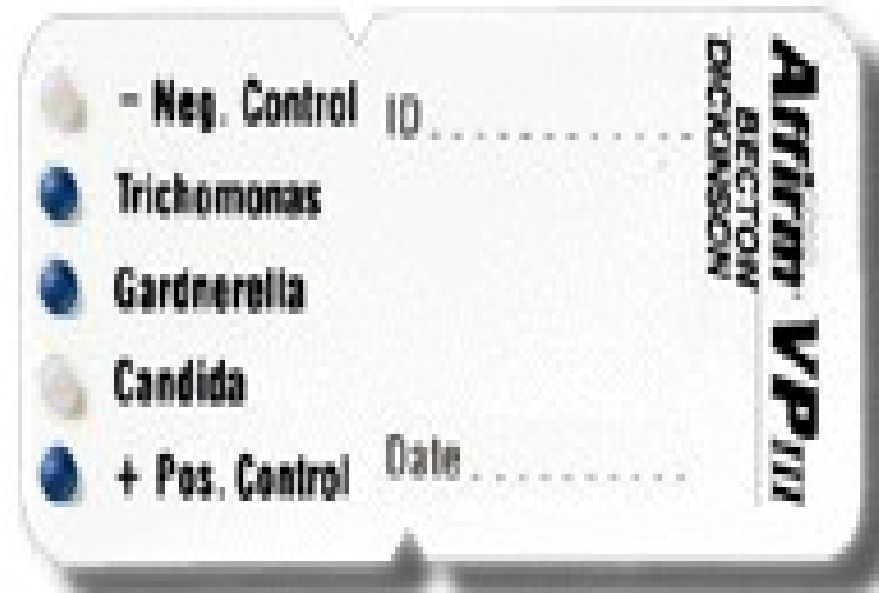
InPouch TV



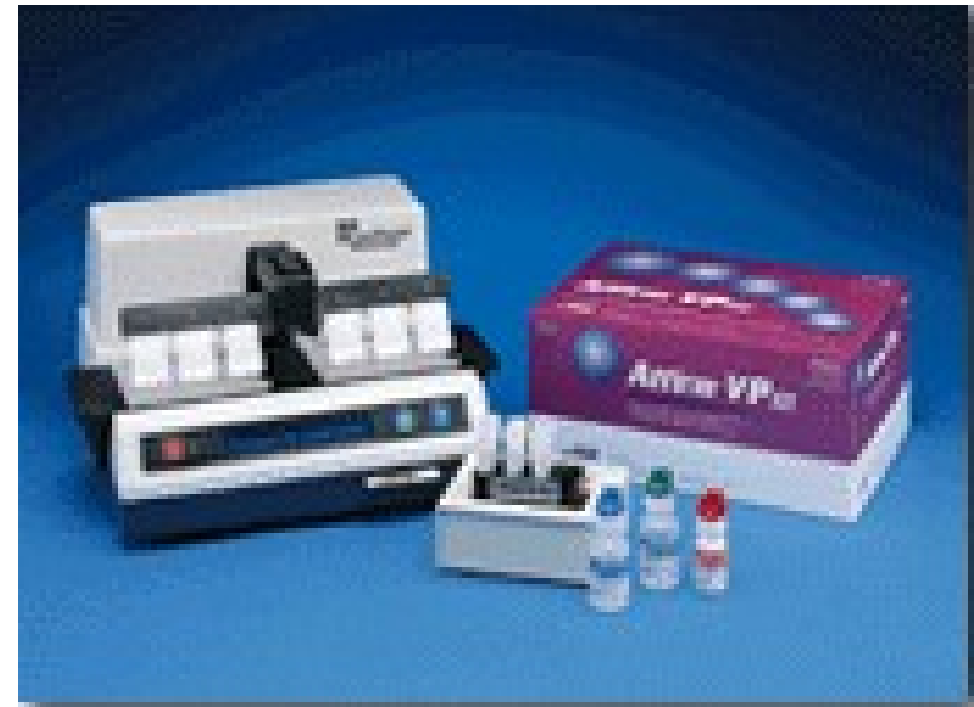
Trich DNA test:

- AffirmVPIII (FDA approved 1997)
- Single sample for yeast, BV and TV
- 90% sensitive, 99% specific (DeMeo, 1996)
 - 44% sens cf to TMA (Sitay,2003)
- Limitations:
 - Cost
 - technology
 - “rapid” 45-60 min...

Affirm VPIII



Easy to perform...easy to read...dependable!



Trich: PCR

- More sensitive than single culture
- Sensitivity 89-97%
- Specificity 88-97%
 - Depends on specimen source, primers, platform
- Limitations
 - Research lab settings
 - Cost and technology

Jordan, 2001, Crucitti 2002
Kaydos, 2002, Kaydos 2003
Van der pol, 2006



Real Time PCR

- Really cool
- Gaydos, Hobbs
- 90% sensitive, 100% specific (urine)
- Expensive!!!!
- Time consuming



Trich TMA

- Genprobe (Aptima) platform, primers, reagents
- Sensitivity 94-96%
- Spec 82-94%
- Abstracts only...



Trich Rapid Antigen Tests

- XenostripTV (FDA Oct 2002) replaced by OSOM® (FDA 2004)
- Immuno-colorimetric antigen detection
- Point of care
- 10 minutes

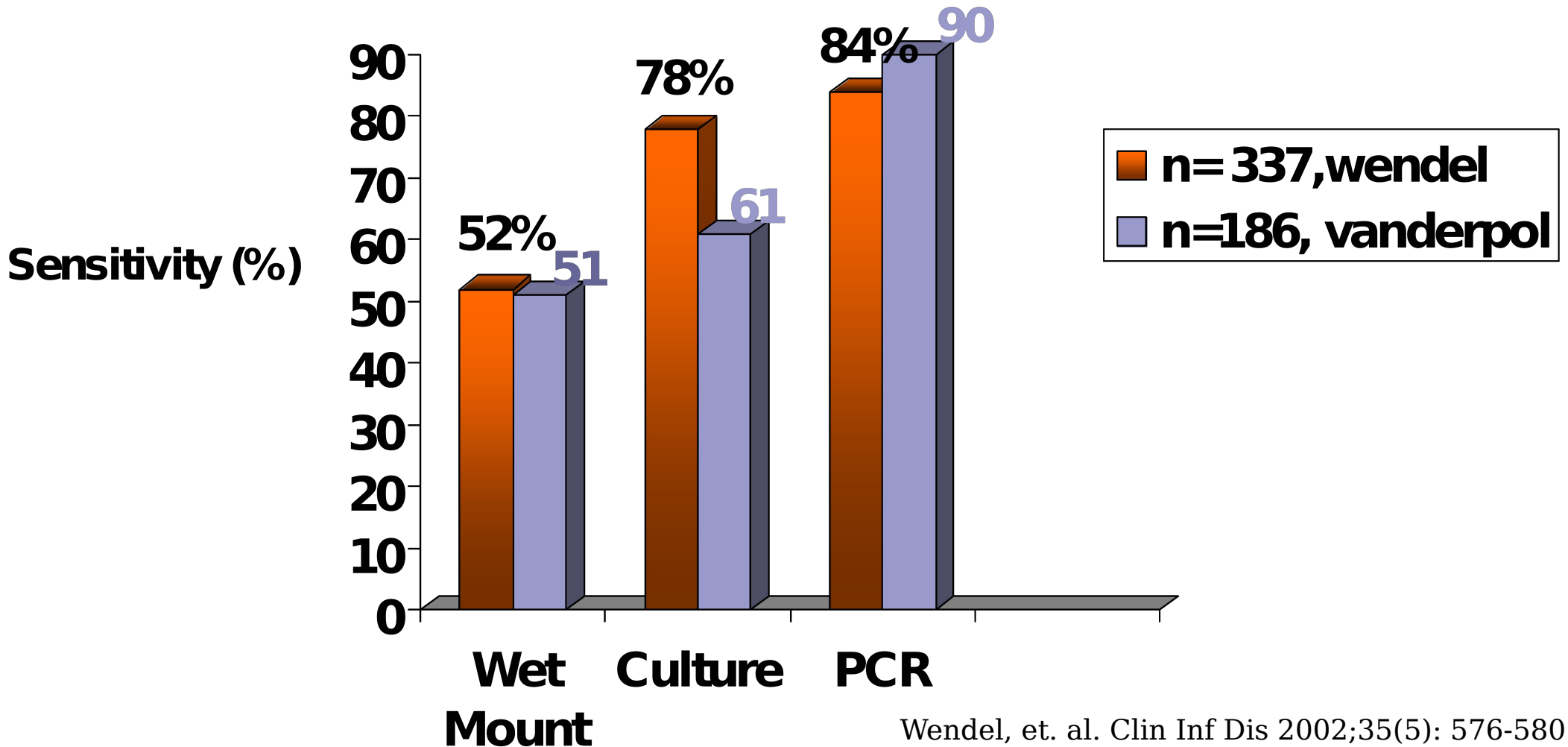
Rapid test research

- Rapid test:
 - 83.3% sensitive
 - 98.8% specific
- Wet mount
 - 71% sensitive, set at 100% specific
- Rapid on used wet mount:
 - 75% sensitive, 98% specific

Comparison of Diagnostic Methods

Method	Cost	Technical ease	Time to Results
Wet Mount	\$	Easy	Minutes
InPouchTV™	\$\$	Easy	Days
Pap Smear	\$\$\$	Moderate	Weeks
PCR	\$\$\$\$	Difficult	Hours-days
Rapid Antigen	\$	Easy	Minutes

Diagnosis of *T. vaginalis* in Females:





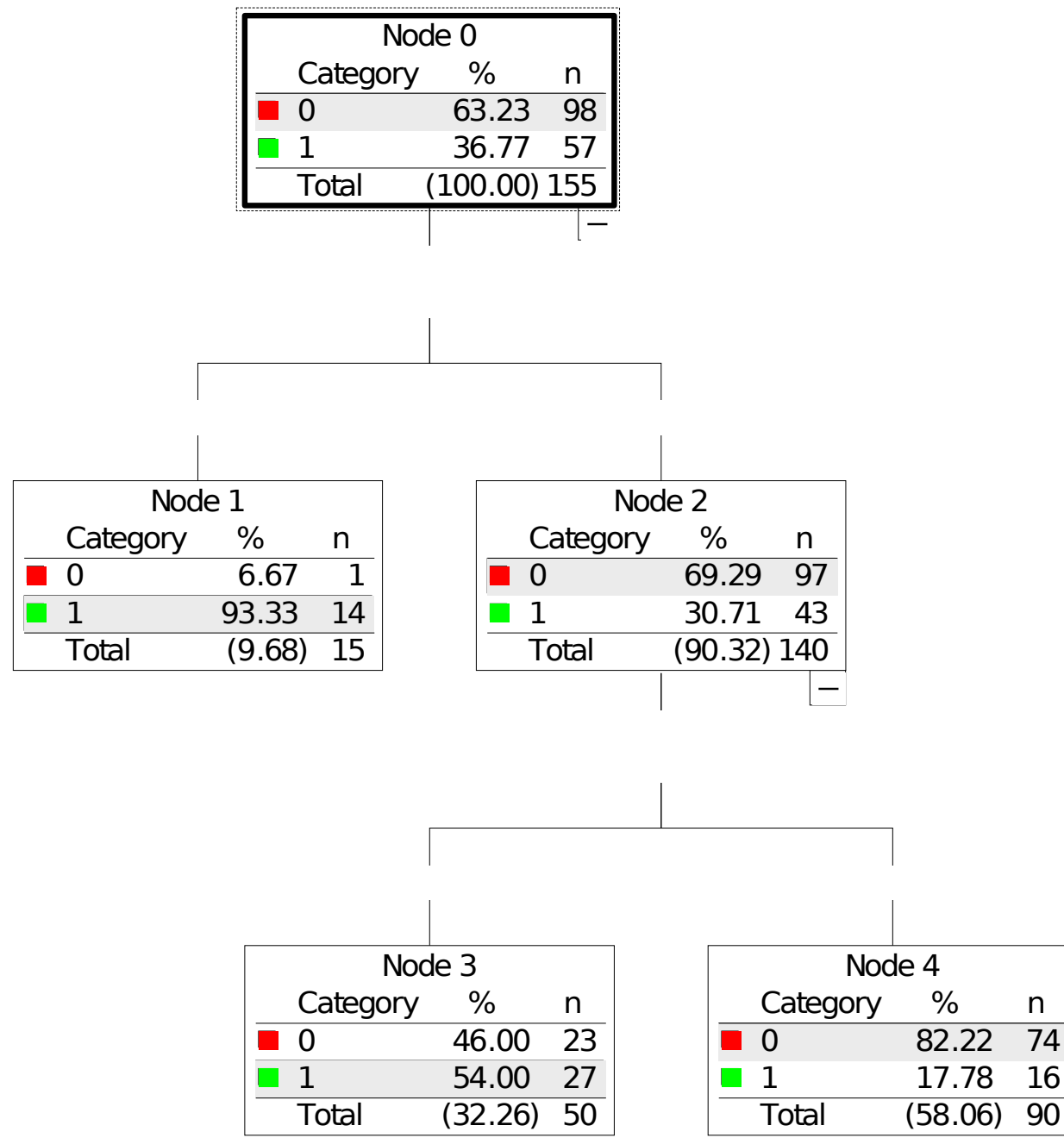
Research Update: Huppert

- STI UTI study: comparison of STIs and UTIs in teen females \pm urinary and vaginal symptoms
- InPouch culture on all (some self collected)
- Results: (N=301)
- Overall Tv prevalence:18%
 - 12% in those who denied vaginal symptoms
 - **33%** with any vaginal symptoms

STI UTI study

- TV not associated with Urinary sx or UTI
- Predictors of TV: OR 95% CI
 - Vaginal symptoms 5.1 1.5-15.1
 - Urine LE+ 8.4 2.7-26.4
 - Urine Blood + 6.3 1.9-21.1
- Sterile pyuria= Tv or GC, not CT
- Wet Prep and UA recommended for females with urinary symptoms

CART



Sens: 74%

Spec: 76%

Huppert, In progress....

- Step-wise evaluation of wetmount , rapid test and culture in symptomatic adolescent females
- 359 adolescent females enrolled
- Overall **17%** prevalence TV
- Rapid test:
 - 93% sens, 98% spec compared to culture
- Awaiting comparison to TMA for TV



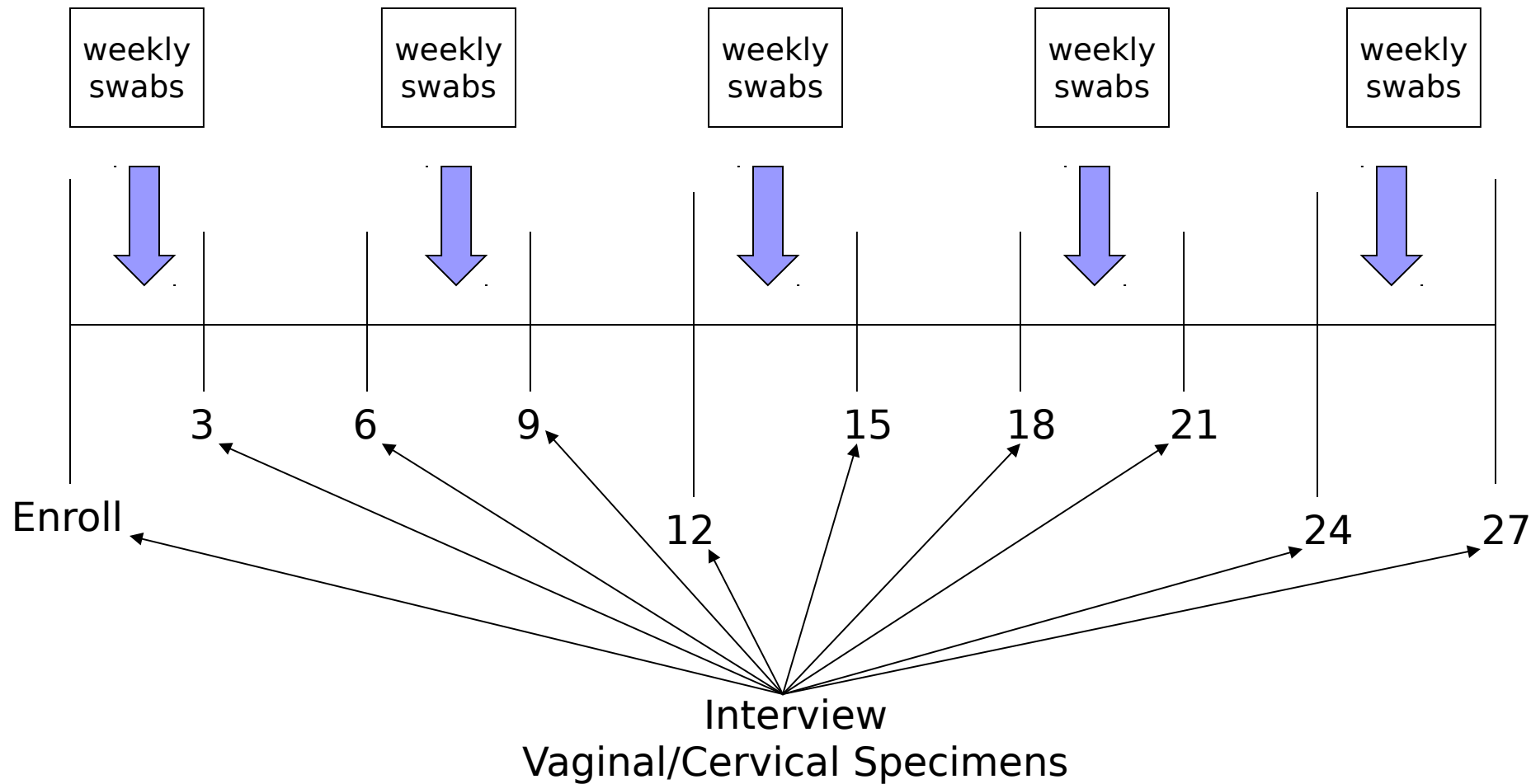
New TV research in Adolescents

- Incidence, Natural History, and Response to Treatment of *Trichomonas vaginalis* among Adolescent Women
 - Van der pol, 2005
- Association of sexual behavior and STIs with duration of genital HPV
 - Shew, 2006



Methods - Participants

- Women receiving health care in three primary health clinics
- Ages 14 to 17 years at enrollment
- Not pregnant at the time of enrollment



Definitions – *T. vaginalis* Infection

- Tv by PCR- TVK (Amplicor)
- Positive sample obtained during enrollment or quarterly clinic visit
- Two positive weekly samples within a single 12-week period
- Single weekly positive visit with additional corroboration (i.e., positive saline wet mount)



Results

- 268 women enrolled
- 245 women with at least 1 follow-up
- 349 women-years of follow-up

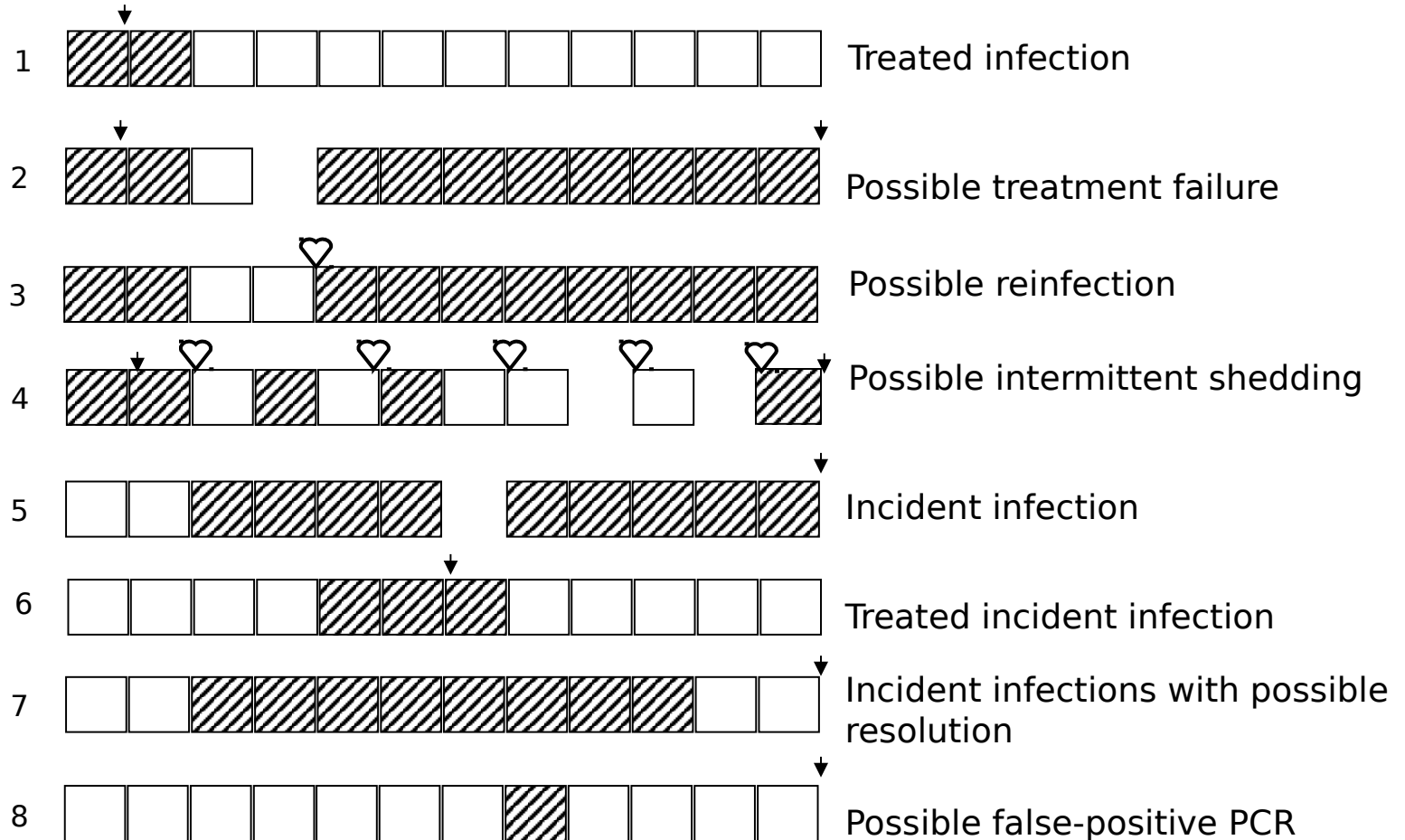


Prevalence & Incidence

- 57/245 (22%) with prevalent/incident infection
- 16/268 (6%) infected at enrollment (prevalent)
- 45/245 (18%) with at least one incident infection
- 18/57 (32%) with multiple infections during follow-up

Pattern

Interpretation





Care Seeking Behaviors and Spontaneous Clearance

- 21 incident infections identified by weekly samples (not identified at the next quarterly visit)
- 11/21 sought treatment
- Median time to treatment = 2 weeks
- 10/21 = spontaneous clearance? Treatment elsewhere?



Response to Treatment

- Treatment documented during 42 weekly collection periods
- 39/42 (93%) negative within two weeks
- Without treatment, longest duration of infection= 12 weeks



Conclusions

- Prolonged duration of untreated infections
- Rapid disappearance of *T. vaginalis* DNA after treatment

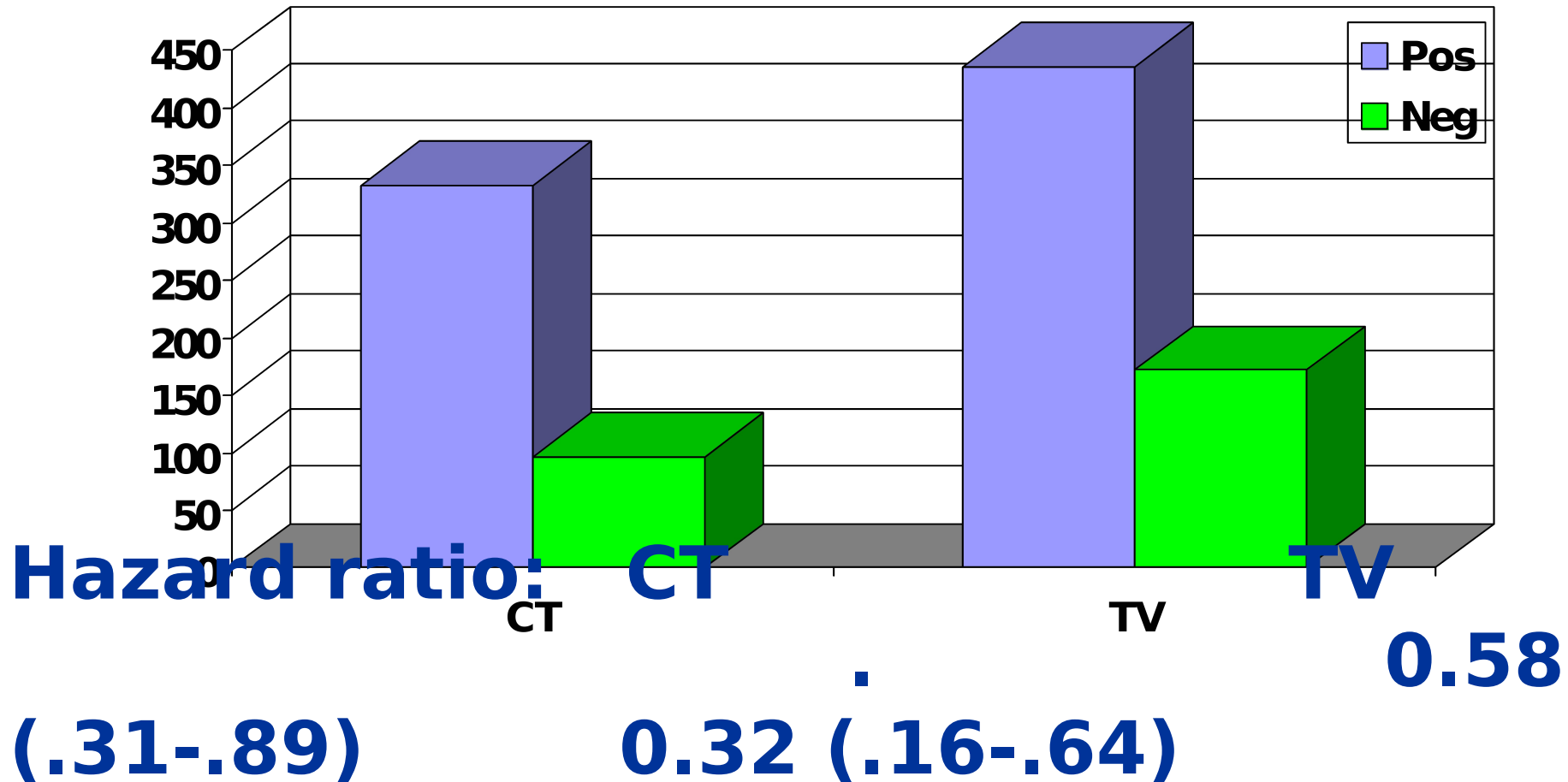
Shew: TV and clearance of HPV

- Longitudinal, weekly samples and quarterly clinical visits, STI testing as described
- HPV typing – PCR-(Roche)
 - 27 types
 - 2 weekly swabs pos for same type= infection
- 49 subjects with 241 HPV infections
- 2458 swabs, 2.2 years of follow-up

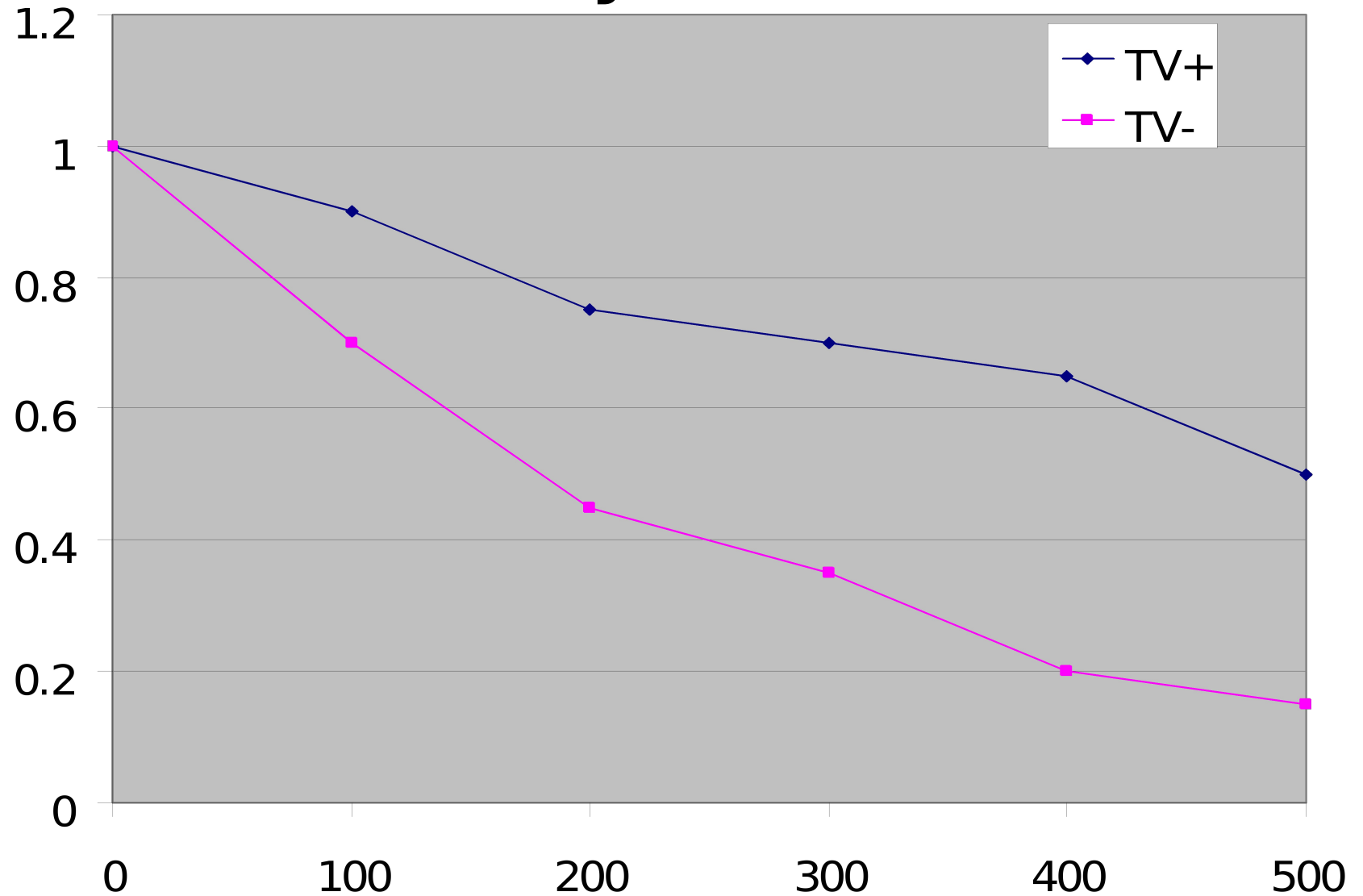
TV and clearance of HPV

<u>Days to clear</u>		<u>Hazard ratio</u>
CT +	CT-	
333	96	0.58 (.31-.89)
TV+	TV-	
436	172	0.32 (.16-.64)

Days to clear HPV infection



Survival of HPV by TV infection





TV and Cervical Cancer

- Not oncogenic
- Biologic plausibility
 - Alter vaginal ecosystem
 - Chronic inflammation
 - Prolongs HPV (see Shew)
- Host response to chronic inflammation



Implications for Practice

Now what should we do?



Implications for Practice

- Who should be screened?
- Which diagnostic method?
- What will better detection of TV accomplish?

Who should be screened?

- Symptomatic women of any age
 - Vaginal complaints
 - Abnormal appearing discharge
- Asymptomatic women at risk of STDs
 - **Teens**
 - >1 sexual partner
 - Substance abuse
 - Other STIs



What TV test method?

- If wet mounts available and reliable:
 - ☐ Wet mount
 - ☐ Culture or rapid test for wet mount negative subjects
- If wet mount not available/reliable
 - ☐ Culture
 - ☐ Rapid test
- If available: PCR/ NAAT

Research directions

- Re-evaluate outcomes using better diagnostic tests
 - PID
 - Obstetric outcomes
 - Cervical neoplasia
 - HIV
 - ?? BV
- Longitudinal studies on effect of TV detection and treatment

Recommended Reading

- Clinical review:

Soper D. Trichomoniasis: under control or undercontrolled? *Am J Obstet Gynecol.* Jan 2004;190(1):281-290.

- Microbiology

Petrin D, Delgaty K, Bhatt R, Garber G. Clinical and microbiological aspects of *Trichomonas vaginalis*. *Clin Microbiol Rev.* 1998;11(2):300-317.



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